IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

AVENTIS PHARMA S.A., SANOFI-AVENTIS U.S., LLC Plaintiffs, v. HOSPIRA, INC., APOTEX, INC., and APOTEX CORP., Defendant.	Civil Action No. 07-721-GMS (Consolidated) **PUBLIC VERSION**

HOSPIRA'S REPLY IN SUPPORT OF ITS SECOND MOTION *IN LIMINE* TO PRECLUDE SANOFI'S EXPERTS FROM TESTIFYING ABOUT THE CLAIM CONSTRUCTION OF "PERFUSION"

Originally Filed: September 21, 2009
Public Version Filed: October 1, 2009

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I. Sanofi's attempt to inject [redacted] additional claim limitations comes too late, and those limitations are impossibly vague.

It is too late now for Sanofi to saddle the single word "perfusion" with three additional limitations – [redacted] referenced nowhere in the claims.

When the parties reached their agreement on perfusion, they agreed to the term's plain meaning as confirmed by the NCI definition – the diluted form of a stock solution that can be infused, and nothing more. Sanofi never raised any of the additional limitations it raising now. For instance, Sanofi's intrinsic evidence chart, submitted in support of its proposed construction, cited nothing suggesting that a perfusion must be [redacted] (*See* Ex. 1, D.I. 44, (Corrected) Joint Claim Construction Chart.)

If it wanted to saddle a single word with those three substantial and indefinite limitations, Sanofi should have raised the issues so that parties could negotiate and, absent agreement, have the issues resolved by this Court at the *Markman* stage For example, [redacted]

Sanofi says that it *implicitly* raised these issues because the agreed definition of "perfusion" includes the used the phrase "suitable for infusion into patients." But as the district court found under virtually identical circumstances in *Medeva Pharms. Mfg., Inc. v. Morton Grove Pharms.*, the equivalent phrase "suitable for oral administration" was "too cryptic and too inartful" to convey to any "objective reader the congeries of meanings now sought to be attributed to that phrase," [redacted]

[redacted] 174 F.Supp.2d 802, 806 (N.D. Ill. 2001). Sanofi's answering brief fails to even address this fundamental point.

In contrast to *Medeva*, Sanofi's cases are inapposite. They all involve the definition of terms that are actually in the claims themselves, unlike here, where Sanofi is adding limitations to the word "suitable," not "perfusion." And they all involve situations where the parties actually *agreed* to add additional requirements to an existing claim term, also unlike here, where Hospira rejects Sanofi's last-minute efforts to saddle a single word with so many undefined limitations. *See, e.g.*, *Amgen v. Hoechst Marion Roussel, Inc.*, 579 F.Supp.2d 199, 206 (D. Mass. 2008) (parties agreed on meaning of "suitable for administration for humans"); *Pharmacia & Upjohn Co. v. Sicor, Inc.*, 447 F.Supp.2d 363, 369 (D. Del. 2006) (counsel "admitted" term "physiologically acceptable" required an injection to be sterile and pyrogen-free); *Purdue Pharma, L.P. v. F.H. Faulding and Co.*, 48 F.Supp.2d 420, 437 (D. Del. 1999) (court finds "there is 'no real dispute' between the parties over what is meant by the phrase 'effective treatment of pain.'").

II. The record confirms that [redacted] are not essential characteristics of a perfusion.

Sanofi also ignores the fact that its own experts and the patent record itself squarely refute its efforts to create new unstated limitations. [redacted]

[redacted] Sanofi's answering brief ignores these critical admissions. [redacted]

Moreover, the '561 patent itself confirms that Sanofi's additional limitations are not proper. For example, [redacted] and there would be no need for the separate limitation "being capable of being injected without causing anaphylactic or alcohol intoxication manifestations." (Id., col. 3, lines 57-60)

III. Hospira's motion to preclude testimony inconsistent with the Court's claim construction is entirely proper.

The cases cited by Sanofi (pp. 4-5) actually ***support*** Hospira's fundamental point that "evidentiary judgments . . . need to be made when such evidence appears to directly clash with the claim construction." *Kemin Foods, L.C. v. Pigmentos Vegetales Del Centro S.A. de C.V.*, No. 4:02-cv-40327, 2004 WL 5508752, at *5 (S.D. Iowa Sept 9, 2004); *accord 3COM Corp. v. Realtek Semiconductor Corp.*, No. C 03-2177 VRW, 2008 WL 783383, at *3 (N.D. Cal. Mar. 24, 2008) (finding no conflict between expert testimony and Court's claim construction). Here, because the conflict between Sanofi's experts' intended testimony and the proper claim construction is clear and substantial, Hospira's motion is ripe for decision.

Dated: September 21, 2009

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EXHIBIT 1

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

AVENTIS PHARMA S.A., SANOFI-AVENTIS U.S., LLC Plaintiffs, v. HOSPIRA, INC Defendant.	)	Civil Action No. 07- 721-GMS

(CORRECTED) JOINT CLAIM CONSTRUCTION CHART

Pursuant to the Court's Scheduling Order (D.I. 20), plaintiffs Aventis Pharma S.A. and sanofi-aventis U.S., LLC, and defendant Hospira, Inc. respectfully submit this corrected Joint Claim Chart in preparation for the claim construction hearing scheduled for March 2, 2009 at 9:30 A.M. **This chart supercedes and replaces the original joint chart filed on December 16, 2008 (D.I. 42).**

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Dated: January 6, 2008

EXHIBIT 2

PATENT
Attorney Docket No.: 3808.0111-01

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

#33
JRP
9/3/97

In re Application of:

Jean-Pierre BASTART et al.

Serial No.: 08/422,672 — Group Art Unit: 1205

Filed: April 12, 1995 — Examiner: T. Criares

For: NEW COMPOSITIONS CONTAINING TAXANE DERIVATIVES

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

RESPONSE AND REQUEST FOR RECONSIDERATION

In response to the Office Action dated January 30, 1997, Applicants respectfully request reconsideration of this application in view of the following remarks. The period for response has been extended three (3) months by the accompanying petition and fee.

Remarks

Interview

Applicants thank the Examiner for the interview held with the undersigned on July 25, 1997. At the interview, the undersigned and Examiner Criares discussed the Tarr reference. Examiner Criares noted that he was willing to consider comparative testing proposed by Applicants but also stated that he

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would favorably consider amendments narrowing the claims to recite the "inventive feature." The Examiner also commented on the similarity between the present application and Serial Nos. 08/398,011 and 08/568,761, which claim priority from the same French patent as the present application. Finally, the Examiner stated his belief that the point of novelty in the present invention is recited in the functional language of the claim, but that he will not give that functional language any weight. The Examiner's concerns will be addressed below.

Rejection Under 35 U.S.C. § 103

Claims 1-5 and 7-12 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Tarr et al. According to the Examiner, Tarr et al. teach Applicants' claimed active compounds and also teach the use of a mixture of ethanol and polysorbate as the carrier. The Examiner states that the differences between the present claims and Tarr are (1) the present claims are limited to a composition consisting essentially of a compound of formula (I) dissolved in a mixture of ethanol and a polysorbate and (2) the amount of active agent. According to the Examiner, the amount of active agent to be added to the carrier would be well within the knowledge of one of ordinary skill in the art.

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Further, the Examiner gives no weight to the functional language "whereby said composition is used to form an injectable solution which contains up to about 1 mg/ml of the compound of formula (I), said injectable solution being capable of being injected without anaphylactic or alcohol intoxication manifestations being associated herewith." His reason for ignoring this language is that the formulation of Tarr would allegedly have the same effect. The Examiner explained his statement at the July 25, 1997 interview, noting that since the composition of Tarr is also diluted and used for injection (see column 4 of Tarr), the functional language does not distinguish over Tarr.

Applicants respectfully traverse the rejection. The presently claimed invention teaches Taxol or a Taxol derivative dissolved in ethanol and polysorbate. The claimed composition is used to form an injectable solution that avoids the problems of anaphylactic shock or alcohol poisoning that may occur when either other solvents or an excess of alcohol is used. See the present specification at, e.g., page 3, lines 3-18, and page 4, lines 3-10.

In contrast, Tarr teaches Taxol dissolved in a three-solvent system: ethanol, polysorbate, and pluronic L64. The three solvents are preferably present in the following amounts: 30% ethanol, 10% polysorbate, 60% pluronic L64.

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As the Examiner knows, the language "consisting essentially of" in Applicants' claim 1 renders the claim open for the inclusion of only unspecified ingredients that do not "materially affect the basic and novel characteristics of the claimed composition." *Atlas Powder Co. v. E.I. DuPont de Nemours & Co.*, 750 F.2d 1569, 1574, 224 U.S.P.Q. 409, 411 (Fed. Cir. 1984). Present claim 1, as written, "consists essentially of" a two-solvent system. For Tarr to render the present claims obvious, the addition of the solvent pluronic L64 would have to not "materially affect the basic and novel characteristics of the claimed composition." However, pluronic L64 constitutes 60% of the solvent system, a considerable percentage. Certainly there is no teaching or suggestion in Tarr that Tarr's composition would work when missing a component which makes up over half of its solvent base. Further, one of ordinary skill in the art would not have had any motivation to remove pluronic L64 from Tarr's solvent system and reasonably expect the system to work.

In addition, Applicants have informed the undersigned that Tarr's system works to solubilize the active principle but that such a system is not recommended for injectable solutions, primarily because it is not sufficiently stable when diluted to form an injectable solution. Applicants have carried out test to show that dilutions of Tarr's disclosed composition with glucose serum to prepare injectable solutions are simply not stable long enough to be useful in

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making perfusions. These assays are summarized in the following tables, which show results for perfusions (diluted solutions) of the compositions of Tarr using Taxol and Taxotere.

6 mg/ml TAXOL SOLUTION* DILUTED IN 5% GLUCOSE SERUM (* solution contains Tarr's three-solvent system: ethanol, polysorbate, and pluronic L64)	
Dosage after Dilution	Visual and/or Microscopic Characterization
0.8 mg/ml	after 3 hours: beginning of crystallization (microscopic characteriz.)
0.6 mg/ml	after 2 hours, 30 minutes: crystallization
0.4 mg/ml	after 3 hours: crystallization
0.2 mg/ml	after 3 hours, 15 minutes: microprecipitation

6 mg/ml TAXOTERE SOLUTION* DILUTED IN 5% GLUCOSE SERUM (* solution contains Tarr's three-solvent system: ethanol, polysorbate, and pluronic L64)	
Dosage after Dilution	Visual and/or Microscopic Characterization
0.8 mg/ml	after 4 hours, 30 minutes: microscopic characterization of crystals
0.6 mg/ml	after 4 hours, 30 minutes: crystallization
0.4 mg/ml	after 4 hours, 30 minutes: microscopic characterization of crystals
0.2 mg/ml	after 4 hours, 30 minutes: crystallization

As shown above, a diluted solution containing 0.8 mg/ml Taxotere and Tarr's three-solvent system (ethanol, polysorbate, and pluronic L64) showed signs of precipitation after 4 hours and 30 minutes. In contrast, a diluted solution

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containing 1.0 mg/ml Taxotere and the presently claimed two-solvent system (ethanol and polysorbate) has been shown to be stable for a sufficient time to be recommended for making perfusions for injection, and is in fact commercially administered as such. See, e.g., present example 3. The solution of Tarr is much less stable as an injectable solution than that of the present invention, and would not be recommended for commercial use in injectable solutions.

These tests firmly support Applicants' position that the presence of pluronic L64 would materially affect the basic and novel characteristics of the claimed composition and thus is excluded from the scope of the present claims. Accordingly, Tarr is not an appropriate reference under 35 U.S.C. § 103 and Applicants respectfully request that the rejection be withdrawn.

Applicants note the Examiner's statement that claims 7-12 would be allowable if the claims were amended to recite the phrase "consisting of" instead of "consisting essentially of." In view of the above arguments, Applicants maintain that such an amendment is not necessary.

Response to Examiner's Comments at Interview

At the July 25, 1997 interview, Examiner Criares expressed concern about the similarities between the present case and other applications in its family. First, Applicants note that they filed a terminal disclaimer in the present case and

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U.S. Patent No. 5,403,858, which is the parent case of the two applications about which the Examiner was concerned, Serial Nos. 08/398,011 and 08/568,761.

Second, with respect to 08/398,011, broad claims 103 and 111 of that application are drawn to a composition and a stock solution, respectively, comprising a taxane derivative dissolved in a surfactant selected from polysorbate and polyethoxylated castor oil, and essentially free or free of ethanol. Claims 156 and 157 of 08/398,011 are drawn to a composition and a stock solution, respectively, comprising a taxane derivative dissolved in a polyethoxylated vegetable oil, and essentially free or free of ethanol. Independent claims 118, 131, 136, and 145 of 08/398,011 recite specific cyclopropyl taxanes dissolved in a surfactant selected from polysorbate and polyethoxylated castor oil and essentially free or free of ethanol. These specific taxanes do not fall within the scope of the present claims. The same applies for independent claims 158-161, except that they are dissolved in polyoxyethylated vegetable oil. Finally, claims 151-155 of 08/398,011 recite compounds comprising specific taxanes dissolved in a surfactant selected from polysorbate and polyethoxylated castor oil, and essentially free or free of ethanol, in which the 7-position, 9-position, 10-position, or 3'-position of the taxanes contains substituents different from those of the presently claimed compounds.

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In contrast, the presently claimed invention is drawn to a composition consisting essentially of a specific compound of formula (I) (Taxol or Taxotere), dissolved in a mixture of ethanol and a polysorbate, whereby the composition is used to form an injectable solution which contains up to about 1 mg/ml of the compound of formula (I) and can be injected without producing anaphylactic shock or alcohol poisoning. Although the Examiner does not give weight to the functional language in the present claims, there is still a distinct difference between the scope of the claims of the 398,011 application and the present claims.

Clearly, these claims overlap but cannot be considered redundant, since, for example, it would be possible to infringe literally claim 103 of the 08/398,011 application without literally infringing claim 1 of the present application. For example, if a composition contains 5 mg/ml of the compound of formula (I) dissolved in the polyethoxylated castor oil and is essentially free or free of ethanol, it could not literally infringe present claim 1 even though claim 103 of 08/398,011 is literally infringed. This "cross-reading" infringement analysis, as explained in *In re Vogel*, 164 U.S.P.Q. 619, 622 (CCPA 1970), demonstrates that these claims are not identical and thus patentable over each other.

Third, the claimed invention in independent claim 18 of 08/568,761 is a composition comprising a specific taxane derivative of the formula (I) dissolved in

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a surfactant selected from polysorbate, polyoxyethylated vegetable oil, and polyethoxylated castor oil, and essentially free or free of alcohol. The same cross-reading infringement analysis applies to demonstrate the separate patentability of this invention.

Finally, Applicants are willing to file a terminal disclaimer over the 08/398,011 and 08/568,761 applications, but do not believe it is necessary.

Conclusion

In light of the above, all of the pending claims are now in condition for allowance. An early and favorable action is earnestly solicited.

To the extent any extension of time under 37 C.F.R. § 1.136 is required to obtain entry of this Amendment, such extension is hereby requested. If there are any fees due under 37 C.F.R. § 1.16 or 1.17 which are not enclosed, including any fees required for an extension of time under 37 C.F.R. § 1.136, please charge those fees to our Deposit Account No. 06-916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P.

By: Thalia V. Warnement
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Reg. No. 39,064

Dated: July 30, 1997

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EXHIBIT 3

Exhibit Redacted in Its Entirety

EXHIBIT 4

US005750561A

United States Patent [19]

Bastart et al.

[11] Patent Number: 5,750,561

[45] Date of Patent: *May 12, 1998

[54] COMPOSITIONS CONTAINING TAXANE DERIVATIVES

[75] Inventors: Jean-Pierre Bastart, Longjumeau; Thierry Dupeyhen, Villemoisson Sur Orge; Jean-Louis Fabre, Paris, all of France

[73] Assignee: Rhone-Poulenc Rorer, S.A., Antony Cedex, France

[*] Notice: The term of this patent shall not extend beyond the expiration date of Pat. No. 5,403,858.

[21] Appl. No.: 422,672

[22] Filed: Apr. 12, 1995

Related U.S. Application Data

[63] Continuation of Ser. No. 980,393, Aug. 4, 1993, abandoned.

[30] Foreign Application Priority Data

Jul. 8, 1991 [FR] France 9108527

[51] Int. Cl.[6] A61K 31/335; A61K 31/34; A61K 9/50

[52] U.S. Cl. 514/449; 514/471; 514/408; 424/502

[58] Field of Search 514/449, 471, 514/408; 424/502

[56] References Cited

U.S. PATENT DOCUMENTS

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5,403,858	4/1995	Bastart et al.	514/449

OTHER PUBLICATIONS

Merck Index, 11th Ed., #7559, (1989), p. 1207.

C.A. 106 (22): 182581c—Tao et al. (1987).

Primary Examiner—Theodore J. Criares

Attorney, Agent, or Firm—Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.

[57] ABSTRACT

The invention provides new compositions containing taxane derivatives, consisting of solutions of such derivatives in a solvent mixture composed of ethanol and polysorbate. These compositions are used to prepare perfusions.

11 Claims, No Drawings

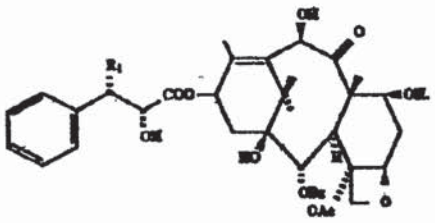
EXHIBIT
Hospira Exhibit
19

JA0033

COMPOSITIONS CONTAINING TAXANE DERIVATIVES

This is a continuation of application Ser. No. 07/930,393, filed on Aug. 4, 1993, now abandoned.

The present invention relates to compositions containing therapeutic agents having antitumour and antileukaemic activity. It relates more especially to pharmaceutical, and in particular injectable, dosage forms containing taxane derivatives, such as, in particular, taxol or one of its analogues or derivatives of the following general formula:



(I)

Wherein R represents a hydrogen atom or an acetyl radical and R_1 represents a tert-butoxycarbonylamino or benzoylamino radical. The two derivatives in which R represents an acetyl group and R_1 a benzoylamino group or in which R represents a hydrogen atom and R_1 a tert-butoxycarbonylamino radical are preferred. The first of these two compounds is better known by the name of taxol, and the second is known by the name of Taxotere.

These products exhibit in vivo substantial activity against malignant tumours, which has enabled them to be studied in the treatment of diseases resistant to other anticancer therapies.

Unfortunately, these products possess such low solubility in water that it has been necessary to prepare a formulation for an injectable preparation based on surfactant and ethanol. Ethanol is the best solvent for dissolving compounds of the formula (I).

As an example, according to the publication by Rowinsky, Lorraine, Cazenave and Donehower which appeared in the Journal of the National Cancer Institute, vol. 82, No. 15, pages 1247–1259 on 1st Aug. 1990, a first solution, termed "stock solution", containing approximately 6 mg/ml of taxol in a solvent mixture composed of:

50% by volume of ethanol

50% by volume of Cremophor EL,

is prepared. For injection, this solution is mixed with a perfusion fluid containing sodium chloride or dextrose. To obtain a mixture which is stable from both a physical standpoint and a chemical standpoint, the authors of this paper state that it is necessary to limit the concentration of active principle in the perfusion solution to concentrations of approximately 0.03 to 0.6 mg/ml (see above publication, page 1251, column 1, third paragraph).

Now, it is desirable to be able to inject sufficient doses of active principle; to this end, clinicians would like to inject concentrations of active principle of between approximately 0.3 and 1 mg/ml in the perfusion fluid; above these doses, anaphylactic shock phenomena which are difficult to control, due in the main to the Cremophor, are seen (see the publication by Rowinsky, page 1250, second column, last paragraph).

This publication also discloses that, to obtain such concentrations (between 0.3 and 1 mg/ml), it is necessary to inject solutions containing, as well as the active principle, concentrations of each of the following compounds, ethanol and most especially Cremophor, of approximately 8 g per 100 ml of solution. Since the treatment often requires the administration of high doses of active principle, and since the concentration of the active principle in the solution is relatively low, the injection of a large volume has the effect of causing, in addition to anaphylactic manifestations, manifestations of alcohol intoxication during the treatment.

It has been discovered that, by the use of the pharmaceutical dosage forms of the present invention, it is possible to avoid the use of Cremophor and greatly to reduce the ethanol concentrations used.

For this purpose, a stock solution is prepared, containing the active principle of formula I in a solvent mixture composed of ethanol, which is the best biocompatible solvent for active principles of this class, and a polysorbate surfactant, e.g. as marketed, in particular, under the name "Tween".

The stock solution is prepared by dissolving the active principle in ethanol and then gradually adding the surfactant. Solutions containing 10 to 100 mg/ml of active principle in a mixture containing approximately 50% of surfactant can be prepared in this manner.

The present invention then makes it possible to replace the Cremophor, described in the publication of the Journal of National Cancer Institute, by a polysorbate. In effect, when an injectable solution containing ethanol and a polysorbate 80 surfactant in place of Cremophor was used in the clinical situation, it became apparent that the anaphylactic reactions were greatly reduced compared with the use of the same solution prepared with Cremophor. In addition to this considerable advantage, it became apparent, most surprisingly, that, in the bottles of stock solution, the concentration of active principle can reach 15 mg/ml. The perfusion fluid after dilution of these bottles contains an amount of ethanol, and also an amount of surfactant, which is reduced a little over twofold.

The perfusions prepared from the above stock solutions, and containing a concentration of active principle of, e.g., 1 mg/ml, which is a preference, or less, contain less than 50 ml/l and preferably less than 35 ml/l of surfactant and of ethanol, which represents a reduction of approximately 40% relative to the perfusions of the prior art.

The new perfusions are stable from a physical standpoint, that is to say no precipitation phenomenon is seen to appear within approximately 8 hours.

The taxol or Taxotere perfusions may be injected into humans at a predetermined flow rate depending on the amount of active principle it is desired to inject. The anaphylactic shock phenomena which were observed with the solutions of the prior art are not observed with these solutions.

The invention is described more completely in the Examples which follow, which are not to be considered as limiting the invention.

EXAMPLES ACCORDING TO THE INVENTION

EXAMPLE 1

Taxotere (0.450 g) is dissolved in ethanol (15 ml). The mixture is made to 30 ml with polysorbate 80 to obtain a solution containing Taxotere (15 mg/ml). The physicochemical stability of this solution is satisfactory.

After mixing with a 5% glucose solution so as to obtain a final concentration of 1 mg/ml, this solution contains 33 ml/l of polysorbate 80 and 33 ml/l of ethanol.

The perfusion is stable for more than 21 hours, i.e. no precipitation phenomenon is seen during this period.

EXAMPLE 2

Example 1 is reproduced with an initial concentration of 10 mg/ml of Taxotere; the results are shown in Table 1.

COMPARATIVE EXAMPLE ACCORDING TO THE PRIOR ART

Taxol (0.180 g) is dissolved in ethanol (15 ml). The mixture is made to volume with Cremophor to obtain a solution (30 ml) which contains taxol (6 mg/ml).

This solution is diluted in the same perfusion solution as above to give a final concentration of 1 mg/ml; the perfusion solution contains 87.7 ml/l of Cremophor and 87.7 ml/l of ethanol. The perfusion solution is stable for more than 21 hours.

EXAMPLE 3

Taxotere (65 g) is dissolved in ethanol (2083 ml). The volume is adjusted to 4147 ml by adding polysorbate 80 (2083 ml). The mixture is homogenized by mechanical stirring. It is filtered through a filter of pore size 0.2 μm. A solution containing Taxotere (approximately 15 mg/ml) is obtained.

After dilution to a Taxotere content of 1 mg/ml in a perfusion bag containing 5% dextrose, this solution is stable for at least 96 hours.

5. A perfusion, which contains approximately 1 mg/ml or less of compound of formula as defined in claim 1, and which contains less than 35 ml/l of ethanol and less than 35 ml/l of polysorbate, wherein said perfusion is capable of being injected without anaphylactic or alcohol intoxication manifestations being associated therewith.

6. A stock solution consisting essentially of a mixture of taxotere and ethanol in a ratio of about 3:100 by weight, and an amount of polysorbate to provide a solution containing about 10 to 15 mg/ml of taxotere, whereby said stock solution is used to form an injectable solution which contains up to about 1 mg/ml of the compound of formula as defined in claim 1, said injectable solution being capable of being injected without anaphylactic or alcohol intoxication manifestations being associated herewith.

7. A perfusion consisting essentially of the stock solution of claim 6 and an amount of glucose solution or dextrose solution to obtain a solution containing about 1 mg/ml of taxotere.

8. A therapeutic composition consisting essentially of a taxane derivative dissolved in a mixture of ethanol and a polysorbate, whereby said therapeutic composition forms or is used to form an injectable solution which contains up to about 1 mg/ml of the compound of formula as defined in claim 1, said injectable solution being capable of being injected without anaphylactic or alcohol intoxication manifestations being associated herewith.

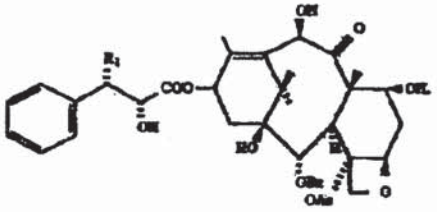
9. The composition of claim 8 wherein said taxane derivative is taxol or an analogue or derivative thereof.

TABLE 1

Example	Product	Solvent	Stock solution concentration	Active principle in the perfusion	Surfactant in the perfusion	Ethanol in the perfusion	Stability
Comparative	taxol	RhOEPCrem	6 mg/ml	1 mg/ml	87.7 ml/l	87.7 ml/l	>21 H
	taxol	RhOEPoly	6 mg/ml	1 mg/ml	83.3 ml/l	83.3 ml/l	>21 H
1	Taxotere	RhOEPoly	15 mg/ml	1 mg/ml	33.3 ml/l	33.3 ml/l	>21 H
2	Taxotere	RhOEPoly	10 mg/ml	1 mg/ml	50 ml/l	50 ml/l	>21 H

We claim:

1. A composition consisting essentially of a compound of formula:



in which R represents a hydrogen atom or an acetyl radical and R_1 represents a tert-butoxycarbonylamino or benzoylamino radical, dissolved in a mixture of ethanol and a polysorbate whereby said composition is used to form an injectable solution which contains up to about 1 mg/ml of the compound of formula I, said injectable solution being capable of being injected without anaphylactic or alcohol intoxication manifestations being associated therewith.

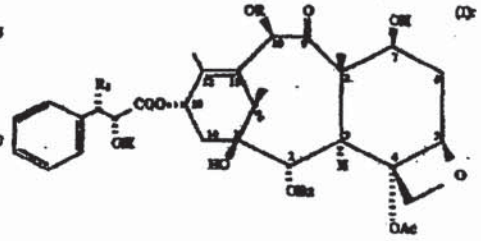
2. A composition according to claim 1, wherein, in the compound of formula (I), R represents a hydrogen atom and R_1 represents a tert-butoxycarbonylamino radical.

3. A composition according to claim 1, wherein, in the compound of formula (I), R represents an acetyl group and R_1 represents a benzoylamino radical.

4. A composition according to claim 1, which contains between 6 and 15 mg/ml of compound of formula (I).

10. The composition of claim 8 wherein said taxane derivative is taxotere or an analogue or derivative thereof.

11. A composition consisting essentially of a compound of formula



in which R represents a hydrogen atom or an acetyl radical and R_1 represents a tert-butoxycarbonylamino or benzoylamino radical,

dissolved in a mixture of ethanol and polysorbate, wherein said ethanol is present in an amount of less than 5% and said polysorbate is present in an amount of less than 5%, said composition being used to form an injectable solution capable of being injected without anaphylactic or alcohol intoxication manifestations being associated herewith.

* * * * *

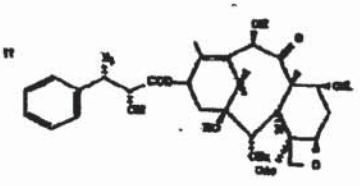
UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

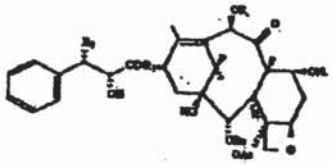
PATENT NO. : 5,750,561
DATED : May 12, 1998
INVENTOR(S) : BASTART et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Claim 1, column 3, lines 43-51, in the formula (I),



" should read —



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Signed and Sealed this

Twenty-seventh Day of April, 1999

Attest:

Q. TODD DICKINSON

Attesting Officer

Acting Commissioner of Patents and Trademarks

JA0036